

### AMENDMENTS TO THE CLAIMS

1. **(Currently Amended)** A method of making an antibody molecule, the antibody containing an immunoglobulin heavy chain comprising a  $\alpha 3$  domain or a mu domain, the method comprising:

(a) Providing a nucleotide sequence encoding the immunoglobulin heavy chain;

(b) Modifying the nucleotide sequence to form a modified nucleotide sequence, wherein the modifying is in the region of the nucleotide sequence encoding the C-terminus 18 amino acids of the completed immunoglobulin heavy chain to remove, or reduce the effectiveness of, one or more vacuolar targeting signal sequences to form a modified nucleotide sequence; of the encoded immunoglobulin heavy chain;

(c) Inserting the modified nucleotide sequence into a host cell; and

(d) Causing the host cell to express the modified nucleotide sequence to form the a modified antibody immunoglobulin heavy chain and secrete the modified antibody immunoglobulin heavy chain from the host cell.

2-33. **(Cancelled)**

34. **(Currently Amended)** A method according to claim 1 wherein the immunoglobulin heavy chain molecule is IgA, IgM or an IgA/G hybrid.

35. **(Currently Amended)** A method according to claim 1 wherein the nucleotide sequence is modified by at least one of the modifications selected from the group consisting of

\_\_\_\_\_ (i) one or more point mutations of the nucleotide sequence,

\_\_\_\_\_ (ii) deleting one or more nucleotides,

\_\_\_\_\_ (iii) adding one or more nucleotides and/or

\_\_\_\_\_ (iv) replacing one or more nucleotides with a synthetic nucleotide sequence.

36. **(Previously presented)** A method according to claim 35, wherein the synthetic nucleotide sequence encodes an amino acid sequence of general formula:

$-(Xaa_1)_m C(Xaa_2)_n$

where: C = a cysteine residue

Xaa<sub>1</sub> = independently any amino acid with the proviso that it is not from I, L or forms a consecutive sequence X<sub>1</sub> X<sub>2</sub> X<sub>3</sub> V S X<sub>4</sub> (SEQ ID NO: 1)

where: X<sub>1</sub> = N, H or L

X<sub>2</sub> = V or Y

X<sub>3</sub> = S or N

X<sub>4</sub> = aliphatic amino acid

Xaa<sub>2</sub> = independently any amino acid

m = at least 2

n = 0 to 5.

37. **(Previously presented)** A method according to claim 36, wherein Xaa<sub>2</sub> is Y and n = 1.

38. **(Currently Amended)** A method according claim 1, wherein nucleotides encoding the last 16 amino acids of the immunoglobulin heavy chain are deleted.

39. **(Currently Amended)** A method according to claim 1 wherein the resultant amino acid sequence at the C terminus of the immunoglobulin heavy chain has a formula selected from the group consisting of:

- (a) SCMVGHEALPMNFTQKTIDRLSGKPACY (SEQ ID NO: 7),
- (b) SCMVGHEALPMNFTQKTIDRLSGKPAAACY (SEQ ID NO: 8),
- (c) SCMVGHEALPMNFTQKTIDRLSGKPHASTPEPDVACY (SEQ ID NO: 9) and
- (d) SCMVGHEALPMNFTQKTIDRLSGKPAAAAACY (SEQ ID NO: 69)

40. **(Currently Amended)** A method according to claim 1 wherein the nucleotide sequence ~~modified of part (a)~~ originally encoded the amino acid sequence:

X<sub>1</sub> X<sub>2</sub> X<sub>3</sub> V S X<sub>4</sub> (SEQ ID NO: 1)

where: X<sub>1</sub> = N, H or L

$X_2$  = V or Y  
 $X_3$  = S or N  
 $X_4$  = aliphatic amino acid.

41. **(Previously presented)** A method according to claim 40, wherein the amino acid sequence is: N V S V S V (SEQ ID NO: 2).

42. **(Currently Amended)** A method according to claim 1 wherein the nucleotide sequence modified of part (a) encoded L or I.

43. **(Currently Amended)** A method according to claim 42, wherein the modified nucleotide sequence encodes a modified amino acid is one or both of selected from the group consisting of:

(i) an isoleucine 3 amino acids and/or 10 amino acids from the C-terminus end of the completed immunoglobulin heavy chain,

(ii) an isoleucine 10 amino acids from the C-terminus end of the immunoglobulin heavy chain and

(iii) an isoleucine 3 amino acids from the C-terminus end of the immunoglobulin heavy chain and an isoleucine to amino acids from the C-terminus end of the immunoglobulin heavy chain.

44. **(Currently Amended)** A method according to claim 1, wherein the method nucleotide sequence ~~modified~~ is contained within a nucleotide sequence encoding the sequence:

P T  $X_1$   $X_2$   $X_3$  V S  $X_4$   $X_5$   $X_6$   $X_7$   $X_8$   $X_9$   $X_{10}$   $X_{11}$   $X_{12}$  C  $X_{13}$  (SEQ ID NO: 5)

where:  $X_1$  = N, H or L, ~~preferably N~~

$X_2$  = V or Y, ~~preferably V~~

$X_3$  = S or N

$X_4$  = an aliphatic amino acid, ~~preferably V or L~~

$X_5$  = an aliphatic amino acid, ~~preferably I, V or L~~

$X_6$  = M, V or L, ~~especially M~~

$X_7$  = S or A

$X_8$  = E or D

$X_9$  = any amino acid, ~~preferably G, V, A or T~~

$X_{10}$  = D, E, G or A, ~~preferably D~~

$X_{11} = \text{G or S, preferably G}$

$X_{12} = \text{I, T, V, Z or A, preferably I or T}$

$X_{13} = \text{may or may not be present and, where present is A or Y}$

45. **(Currently Amended)** A method of adding J-chain binding capability to the immunoglobulin heavy chain of an antibody comprising the steps of:

- (a) providing a nucleotide encoding an immunoglobulin heavy chain;
- (b) adding to that nucleotide a nucleotide sequence encoding a synthetic tail with the amino acid sequence:

$-(\text{Xaa}_1)_m \text{C}(\text{Xaa}_2)_n$

where: C = Cys

Xaa<sub>1</sub> is independently any amino acid with the proviso that it is not I or L or forms a consecutive sequence X<sub>1</sub> X<sub>2</sub> X<sub>3</sub> V S X<sub>4</sub> (SEQ ID NO: 1) (where X<sub>1</sub> = N, H or L; X<sub>2</sub> = V or Y; X<sub>3</sub> = S or N; X<sub>4</sub> = aliphatic amino acid)

Xaa<sub>2</sub> = independently any amino acid

m = at least 2

n = 0 to 5; and

- (c) expressing the ~~completed~~ immunoglobulin nucleotide in a host cell to form an immunoglobulin heavy chain capable of binding J-chain.

46. **(Previously presented)** A method according to claim 1 wherein the host cell is a plant cell.

47. **(Previously presented)** A method according to claim 45 wherein the host cell is a plant cell.

48. **(Previously presented)** A method according to claim 46, wherein the plant cell is part of a transgenic plant.

49. **(Previously presented)** A method according to claim 47, wherein the plant cell is part of a transgenic plant.

50. **(Previously presented)** A method according to claim 1 additionally comprising the step of isolating and purifying the antibody molecule.

51. **(Previously presented)** A method according to claim 45 additionally comprising the step of isolating and purifying the antibody molecule.

52. **(Currently Amended)** A method according to claim 50, wherein the antibody molecule is subjected to a protease digest to ~~for~~produce Fab or F(ab')<sub>2</sub> fragments.

53. **(Previously presented)** A method according to claim 51, wherein the antibody is subjected to a protease digest to for Fab or F(ab')<sub>2</sub> fragments.

54. **(Currently Amended)** An antibody containing an immunoglobulin heavy chain comprising an  $\alpha 3$  domain or a mu domain, the  $\alpha 3$  domain or mu domain lacking one or more targeting signals towards the C-terminal end.

55. **(Previously presented)** An antibody capable of binding J-chain comprising at its C-terminal end the sequence:

$-(Xaa_1)_m C(Xaa_2)_n$

where: C = Cys

Xaa<sub>1</sub> is independently any amino acid with the proviso that it is not I or L or forms a consecutive sequence X<sub>1</sub> X<sub>2</sub> X<sub>3</sub> V S X<sub>4</sub> (SEQ ID NO: 1) (where X<sub>1</sub> = N, or L; X<sub>2</sub> = V or Y; X<sub>3</sub> = S or N; X<sub>4</sub> = aliphatic amino acid)

Xaa<sub>2</sub> = independently any amino acid

m = at least 2

n = 0 to 5

56. **(Previously presented)** An antibody according to claim 54 which does not contain the targeting signal: X<sub>1</sub> X<sub>2</sub> X<sub>3</sub> V S X<sub>4</sub> (SEQ ID NO: 1)

where: X<sub>1</sub> = N, H or L

$X_2 = V \text{ or } Y$   
 $X_3 = S \text{ or } N$   
 $X_4 = \text{aliphatic amino acid.}$

57. **(Previously presented)** An antibody according to claim 55 which does not contain the targeting signal:  $X_1 X_2 X_3 V S X_4$  (SEQ ID NO: 1)

where:  $X_1 = N, H \text{ or } L$   
 $X_2 = V \text{ or } Y$   
 $X_3 = S \text{ or } N$   
 $X_4 = \text{aliphatic amino acid.}$

58. **(Previously presented)** An antibody according to claim 56, wherein the targeting signal is  $N V S V S V$  (SEQ ID NO: 2).

59. **(Previously presented)** An antibody according to claim 57, wherein the targeting signal is  $N V S V S V$  (SEQ ID NO: 2).

60. **(Previously presented)** An antibody according to claim 54 which contains one or no isoleucine or leucine amino acids within the last 18 amino acids at the C-terminus of the heavy chain of the antibody.

61. **(Previously presented)** An antibody according to claim 55 which contains one or no isoleucine or leucine amino acids within the last 18 amino acids at the C-terminus of the heavy chain of the antibody.

62. **(Previously presented)** An antibody according to claim 54 comprising at the C-terminus end of the heavy chain of antibody, the sequence:

$-(Xaa_1)_m C(Xaa_2)_n$

where: C = cysteine residue

$Xaa_1 = \text{independently any amino acid with the proviso that it is not I or L}$   
 $\text{or forms a consecutive sequence } X_1 X_2 X_3 V S X_4 \text{ (SEQ ID NO: 2)}$

where:  $X_1 = N, H \text{ or } L$

$X_2 = V \text{ or } Y$

$X_3 = \text{S or N}$

$X_4 = \text{aliphatic amino acid}$

$Xaa_2 = \text{independently any amino acid}$

$m = \text{at least 2}$

$n = 0 \text{ to } 5.$

63. **(Previously presented)** An antibody according to claim 55 comprising at the C-terminus end of the heavy chain of antibody, the sequence:

$-(Xaa_1)_m C(Xaa_2)_n$

where: C = cysteine residue

$Xaa_1 = \text{independently any amino acid with the proviso that it is not I or L}$   
or forms a consecutive sequence  $X_1 X_2 X_3 V S X_4$  (SEQ ID NO: 2)

where:  $X_1 = \text{N, H or L}$

$X_2 = \text{V or Y}$

$X_3 = \text{S or N}$

$X_4 = \text{aliphatic amino acid}$

$Xaa_2 = \text{independently any amino acid}$

$m = \text{at least 2}$

$n = 0 \text{ to } 5.$

64. **(Previously presented)** An antibody according to claim 54 in which at least two, preferably two to four, glycine or alanine residues are present downstream of a C-terminal targeting sequence

65. **(Previously presented)** An antibody according to claim 55 in which at least two, preferably two to four, glycine or alanine residues are present downstream of a C-terminal targeting sequence

66. **(Previously presented)** An antibody according to claim 54 in which at least the terminal amino acid residue of a C-terminal targeting sequence is replaced by at least two, preferably two to four, glycine or alanine residues.

67. **(Previously presented)** An antibody according to claim 55 in which at least the terminal amino acid residue of a C-terminal targeting sequence is replaced by at least two, preferably two to four, glycine or alanine residues.
68. **(Previously presented)** A method of treating a disease by administering an antibody according to claim 54 to a patient.
69. **(Previously presented)** A method of treating a disease by administering an antibody according to claim 55 to a patient.
70. **(Previously presented)** A method of prophylaxis, comprising administering an antibody according to claim 54 to a person or animal.
71. **(Previously presented)** A method of prophylaxis, comprising administering an antibody according to claim 55 to a person or animal.
72. **(Previously presented)** A vector comprising a nucleotide sequence encoding an antibody according to claim 54.
73. **(Previously presented)** A vector comprising a nucleotide sequence encoding an antibody according to claim 55.
74. **(Previously presented)** A host cell comprising a nucleotide sequence encoding antibody according to claim 54.
75. **(Previously presented)** A host cell comprising a nucleotide sequence encoding antibody according to claim 55.
76. **(Previously presented)** A host cell comprising a vector according to claim 72.
77. **(Previously presented)** A host cell comprising a vector according to claim 73.



78. **(Previously presented)** A transgenic plant comprising a nucleotide encoding an antibody according to claim 54.

79. **(Previously presented)** A transgenic plant comprising a nucleotide encoding an antibody according claim 55.

80. **(Previously presented)** An immunoassay comprising an antibody as defined in claim 54.

81. **(Previously presented)** An immunoassay comprising an antibody as defined in claim 55.

82. **(Currently Amended)** The method of claim 1, further comprising adding to the nucleotide sequence encoding the immunoglobulin heavy chain a nucleotide sequence encoding a synthetic tail with the amino acid sequence  $-(Xaa_1)_m C(Xaa_2)_n$ , wherein:

- C = Cys
- $Xaa_1$  is independently any amino acid with the proviso that it is not I or L or forms a consecutive sequence  $X_1 X_2 X_3 V S X_4$  (where  $X_1 = N, H$  or  $L$ ;  $X_2 = V$  or  $Y$ ;  $X_3 = S$  or  $N$ ;  $X_4 =$  aliphatic amino acid)
- $Xaa_2 =$  independently any amino acid
- $m =$  at least 2
- $n = 0$  to 5; and

wherein said synthetic tail adds J-chain binding capability to the heavy chain of the immunoglobulin.

83. **(Previously presented)** A method according to claim 82 wherein the host cell is a plant cell.

84. **(Previously presented)** A method according to claim 83, wherein the plant cell is part of a transgenic plant.

85. **(Previously presented)** A method according to claim 82 additionally comprising the step of isolating and purifying the antibody molecule.

86. **(Currently Amended)** A method according to claim 85, wherein the antibody molecule is subjected to a protease digest to ~~for produce~~ Fab or F(ab')<sub>2</sub> fragments.

87. **(New)** The method according to claim 44, wherein at least one of X<sub>1</sub>-X<sub>13</sub> is selected from the group consisting of:

X<sub>1</sub> = N

X<sub>2</sub> = V

X<sub>4</sub> = V or L

X<sub>5</sub> = I, V or L

X<sub>6</sub> = M

X<sub>9</sub> = G, V, A or T

X<sub>10</sub> = D

X<sub>11</sub> = G

X<sub>12</sub> = I or T.